

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
7 October 2004 (07.10.2004)

PCT

(10) International Publication Number
WO 2004/084824 A3

(51) International Patent Classification⁷: C07D 213/26, 213/55, 213/56, 239/26, 401/04, 403/04, A61K 31/4418, 31/4436, 31/505, 31/506

(74) Common Representative: MERCK & CO., INC.; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(21) International Application Number:
PCT/US2004/008532

(22) International Filing Date: 19 March 2004 (19.03.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/456,312 24 March 2003 (24.03.2003) US

(71) Applicant: MERCK & CO., INC. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): CHAKRAVARTY, Prasun, K. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). FISHER, Michael, H. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). PARSONS, William, H. [US/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). LIANG, Jun [CN/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US). ZHOU, Bishan [CN/US]; 126 East Lincoln Avenue, Rahway, NJ 07065-0907 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
31 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: BIARYL SUBSTITUTED 6-MEMBERED HETEROCYCLES AS SODIUM CHANNEL BLOCKERS

(57) Abstract: Biaryl substituted pyridine, pyrimidine and pyrazine compounds are sodium channel blockers useful for the treatment of pain. Pharmaceutical compositions comprise an effective amount of the instant compounds, either alone, or in combination with one or more therapeutically active compounds, and a pharmaceutically acceptable carrier. Methods of treating conditions associated with, or caused by, sodium channel activity, including, for example, acute pain, chronic pain, visceral pain, inflammatory pain, neuropathic pain, epilepsy, irritable bowel syndrome, depression, anxiety, multiple sclerosis, and bipolar disorder, comprise administering an effective amount of the present compounds, either alone, or in combination with one or more other therapeutically active compounds.

WO 2004/084824 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/08532

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07D 213/26, 213/55, 213/56, 239/26, 401/04, 403/04; A61K 31/4418, 31/4436, 31/505, 31/506
 US CL : 546/323, 326, 346, 348; 544/122, 323, 335; 514/235.8, 256, 275, 277, 354, 355, 356

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 546/323, 326, 346, 348; 544/122, 323, 335; 514/235.8, 256, 275, 277, 354, 355, 356

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,873,248 A (KATOH et al) 10 October 1989 (10.10.1989), see formula (I), especially compounds in Table 1.	1, 12, 18, 19, 24, 27, 44
X	WO 01/81312 A2 (MERCK FROSST CANADA & CO.) 01 November 2001 (01.11.2001), see formula in Table 1, especially compounds 5, 47 and 49.	1-3, 5-9, 11, 44-58
X	US 4,783,466 A (KATOH et al) 08 November 1988 (08.11.1988), see formula (I), especially compounds in Table 1.	1, 12, 14, 29, 44

Further documents are listed in the continuation of Box C.

See patent family annex.

Special categories of cited documents:

- “A” document defining the general state of the art which is not considered to be of particular relevance
- “E” earlier application or patent published on or after the international filing date
- “L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- “O” document referring to an oral disclosure, use, exhibition or other means
- “P” document published prior to the international filing date but later than the priority date claimed

“T”

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X”

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y”

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&”

document member of the same patent family

Date of the actual completion of the international search

18 October 2004 (18.10.2004)

Date of mailing of the international search report

06 JAN 2005

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
 Commissioner of Patents
 P.O. Box 1450
 Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Deepak Rao

Telephone No. 571-272-1600

DEBORAH A. THOMAS
 PARALEGAL SPECIALIST
 GROUP 1300